A STUDY OF ISODEHYDROACETIC ESTER

BY

EUGENE MILLER McCOLM

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THIS IS TO CERTIFY THAT THE THESIS PREPARED UNDER MY SUPERVISION BY

Eugene Miller McColm

ENTITLED A STUDY OF ISODEHYDRACETIC ESTER

IS APPROVED BY ME AS FULFILLING THIS PART OF THE REQUIREMENTS FOR THE

DEGREE OF Bachelor of Science in Chemical Engineering.

S. L. Souther
Instructor in Charge

APPROVED: W. A. Noyes

HEAD OF DEPARTMENT OF Chemistry

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E. M. M.

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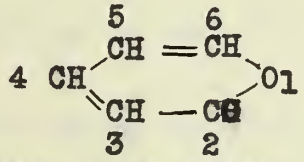
I

LITERATURE

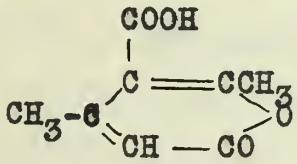
A. Preparation of the Ester.

An α-pyrone is a cyclic compound having an oxygen atom in the ring and an oxygen atom on the α carbon atom. It has the following structure:-



The atoms are numbered as shown.

Isodehydroacetic acid is the dimethyl cumalinic acid in which the methyl groups are on the fourth and sixth carbon atoms. It has the following structure:-



The ester that was studied was the ethyl ester of this acid.

To prepare the acid and ester the following method was used[1]. "According to Hantzsch the first condensation product is formed by the action of sulfuric acid on acetoacetic ester. It crysatallizes from ether in compact crystals, and from water

[1] Liebig's Annalen, V. 259, p. 151.

in loose, soft crystals resembling asbestus. In both cases it is pure for its melting point is not changed by recrystallizing from hot water. It reacts, after freeing from sulfuric acid, extreemly acid. It breaks up in alcoholic potash to the potassium salt of the acid (isodehydroacetic) and to the ethyl ester of this acid.

According to this the condensation product may be regarded as an ether of the acid and ester. After the breaking up of the lactone ring, both substances are thought to be formed by the addition of two molecules of water.

To prepare the ester it is not necessary to recrystallize the first condensation product, nor to use the alcoholic potash. The best plan is to dissolve the product, after filtration, in a solution of ether and chloroform which is lighter than water to allow washing with ease. This solution is washed with water several times to remove the sulfuric acid, and is then shaken with a concentrated solution of potash. The potassium salt of the acid will be found in the potash layer and the ester will be in the ether-chloroform layer. The acid is recovered merely by neutralizing the potash with hydrochloric acid when the isodehydroacetic acid will be precipitated. The ester is recovered pure by diminished pressure distillation of the ether chloroform solution.

130 grams of the acid, and 190 grams of the ester were obtained in this manner from a liter of acetoacetic ester."

The following additions were made to the above.[1]

"The sulfuric acid and the acetoacetic ester must be mixed slowly and with cooling, and allowed to stand from ten to fourteen days. When a little of this solution mixed with ice and water gives a heavy, turbid precipitate, the solution is ready to be worked up. It is poured into a mixture of ice and water that has three times the weight of the solution and allowed to stand for twentyfour hours. It is then filtered."

The method that I used was a little different from the above.

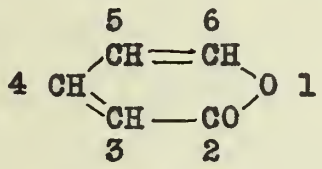
Another method for the preparation of the ester alone is by the use of hydrochloric acid. According to this method[2] acetoacetic ester is saturated with dry hydrogen chloride at the temperature of ice. The mixture is then allowed to stand for a month at the above temperature and is then fractioned under diminished pressure. Hembd obtained a yield of 420 grams of isodehydroacetic ester from a kilo of acetoacetic ester.

[1] Elbs, II, p. 248

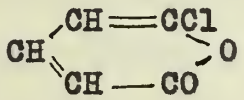
[2] Beilstein, I, p. 776; and Hembd, Thesis at Kiel, Ger., 1914.

B. Preparation of the chlor α-pyrones.

For convenience the formula of the simplest of the α-pyrones, mesityn, is given again, with the carbon atoms numbered as shown.



Bland and Thorpe give the following preparations:- [1]
6-chloro α-pyrone is obtained when glutaconic acid is treated with acetyl chloride in the presence of phosphorous trichloride. The chlor pyrone formed has the following formula:-



6-chlor 4-methyl α-pyrone is formed by the reaction of acetyl chloride with 6-hydroxy 4-methyl α-pyrone.

Genveresse[2] gives a method for the chlorination of isodehydroacetic ester (ethyl). In this method the ester is cooled to 0° and the equivalent amount of sulfuryl chloride is added drop by drop. When the reaction is complete crystals of the chlorinated ester form in the liquid. These are dissolved in ether and the solvent evaporated in a vacuum over sulfuric acid. If this chlor ester is heated with hydrochloric acid in a sealed tube to 250°, carbon dioxide, ethyl acetate, and chlormethyl ether are formed. If this is so the chlorine was present on one of the methyl groups.

[1]Jour. Chem. Soc. 101, 856-70 [2]Annales de Chimie V.24, ser.6,p.98

Oppenheim and Precht[1] have another method for the preparation of the above chlor acid. In this method a mixture of chlorine in chloroform and a chloroform solution of isodehydroacetic acid are allowed to stand for a half hour. The chlor acid crystallizes immediately into small needles that are soluble in alcohol and melt at 93° C. On longer standing, six hours or more, a syrupy liquid forms which has not yet been identified.

Pechmann and Mills[2] give a method for the chlorination of the methyl ester of cumalinic acid. To prepare this chlor ester a mixture of the pure ester of the acid is allowed to stand with a solution of chlorine in carbon tetrachloride. After two or three days hydrochloric acid begins to come off, crystals form, and the solution bleaches out. When free chlorine is no longer present the crystals are filtered and washed with ether. The melting point, after recrystallization from alcohol, is 134-136° C.

Feist[3] gives a method for the chlorination of isodehydroacetic ester. The chlor ester is formed by the reaction of the ester with sulfuryl chloride at the temperature of ice. Ether is used as the solvent. The product is white and crystallineand melts at 57°.

Thole and Thorpe[4] give methods for the preparation of seven-

[1] Berichte V. 9, p. 1101.

[2] Ibid V. 37, p. 3831

[3] Annalen V. 345, p. 74.

[4] Jour. Chem. Soc. V. 99, p. 2208

al of the chlor α-pyrones.

6-chloro 3-methyl α-pyrone is prepared by boiling methyl glutaconic acid with acetyl chloride. Melting point 71° C.

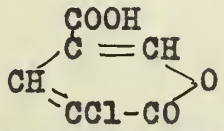
The similar ethyl pyrone is formed in the same manner by treating the ethyl glutaconic acid in the same way. It has a melting point of 39° and a boiling point of 133°.

The similar benzyl pyrone is formed by boiling 6-hydroxy 3-benzyl α-pyrone with acetyl chloride. It has a melting point of 74°.

6-chloro 3,4-dimethyl α-pyrone is formed by heating dimethyl glutaconic acid with two moles of acetyl chloride in a sealed tube at 100° for ten hours.

The chlor anhydride of the trimethyl glutaconic acid cannot be formed in the same manner.

Pechmann and Mills[1] have a method for the preparation of chlor cumalinic acid. It is formed by the action of chlorine in an acetic acid solution of the acid in the presence of iodine. It has the following structure:-



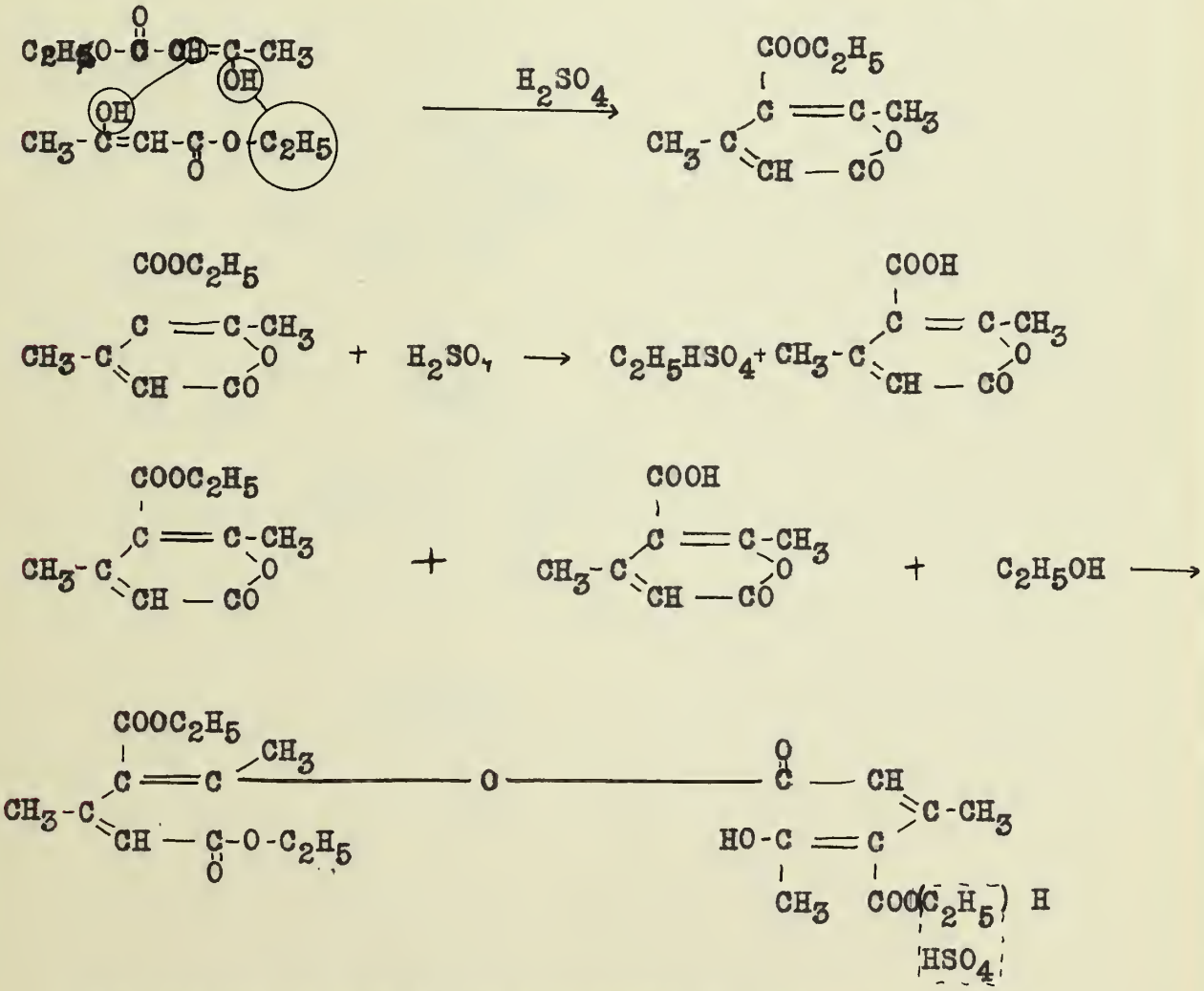
This structure is assumed since it can be converted into 3-chloro pyridene. Its melting point is 187°.

[1]Berichte V. 37, p. 3829

II

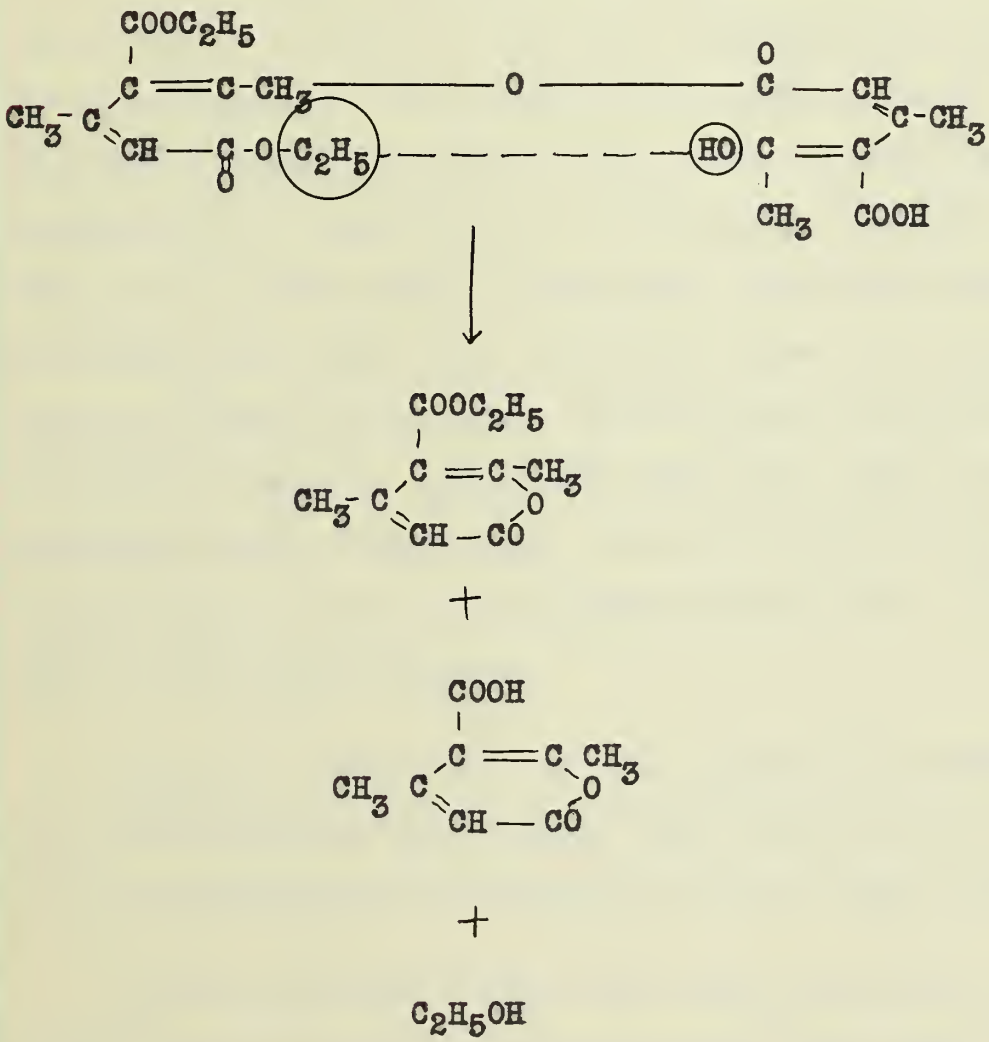
Reactions

It is supposed that acetoacetic ester condenses in the presence of sulfuric acid in the following manner: Two molecules of the ester condense to isodehydroacetic ester. Part of the latter is then hydrolized by sulfuric acid to form isodehydroacetic acid. A molecule of the latter then reacts with a molecule of the ester to form an ether of the acid and ester which is the first condensation product. The reaction is carried out in the following manner.



The latter is the first condensation product.

It further loses a molecule of alcohol and breaks up into a molecule of the acid and one of the ester. This breaking up is the reverse of its formation. It occurs when the potash is added to the solution of the condensation product in ether and chloroform.



III

EXPERIMENTAL WORK

A. Preparation of the acid and ester.

The Sulfuric Acid Method

The method used was slightly different from that given above in the literature. The first condensation product was filtered as above and the filtrate was extracted with the ether-chloroform mixture to recover any of the product that was dissolved in it. After the layer containing the potassium salt of the acid had been separated from the ether-chloroform layer containing the ester, the latter was dried over calcium chloride and the solvent boiled off. The remainder was distilled under diminished pressure. The first thing that came over was a little unchanged ester. Then came a trace of mesityn lactone and following this the ester of isodehydroacetic acid. It comes off at 200° C. at 50 mm. pressure.

The acid is recovered by neutralizing the potash solution with hydrochloric acid (dilute) and filtering the precipitate. It is recrystallized by throwing it out of ether with ligroin.

In all the methods that were tried the first condensation product was not allowed to stand twenty four hours after precipitation and before filtration, as Hantzsch did[1].

Preparation A:- The above method was used except that the mixture of acetoacetic ester and sulfuric acid was only allowed to stand for four hours at a constant temperature of 35° C. The yield was 17 g. of the ester coming over at 190-195° C. The acid was not worked up.

[1] This work, p.3

Preparation B:- The same method as above was used except that the mixture was allowed to stand for fourteen days at room temperature.

Yield:- 20 grams of the ester at 190-195° at 40 mm. pressure.

7 grams of the pure acid. Melting point 149°

Preparation C:- Same method as in B

Yield: 7 grams of the ester at 190° at 40 mm. pressure.

The acid was not worked up.

Preparation E:- Same method as in B.

Yield:- 10 grams of the ester at 198° at 50 mm. pressure.

18 grams of the acid. Melting point 148°

Preparation G:- Same method as in B.

Yield:- 10 grams of the ester at 195° and 40 mm. pressure.

The acid was not worked up.

In this preparation was allowed to stand for twenty four hours to discover whether that would increase the yield. It did not do so.

Preparations I, and J:- Same method as in G.

Yield of each:- 10 grams of the ester.

15g. of the acid.

The Hydrochloric Acid Method

The method of preparation has already been described on page 3 of the thesis. It was followed exactly as given.

Preparation D:- 100 grams of acetoacetic ester were saturated with dry hydrogen chloride at the temperature of ice. The solution turned brown after the hydrogen chloride had been passing into it for a short time. It was allowed to stand at the temperature of ice for a month and was then fractioned. In this method there was none of the acid formed. The yield of ester, distilling at 195° at 43 mm. pressure, was 43 grams. 30 grams of an unknown substance came over at 50° and at 80 mm. pressure. This unknown was later fractioned at atmospheric pressure with the following results: There were two fractions, one coming off at 87-94°, and the other at 240°. There was only a small amount of the latter and it was evidently isodehydroacetic ester from its smell and boiling point. The first fraction precipitated the silver chloride immediately on a test wit h silver nitrate. this showed that the chlorine present was present in an inorganic compound. Since the only things possible were water, alcohol, and hydrochloric acid it was assumed that the unknown was a mixture of these three constituents with a very little acetoacetic ester.

Preparation F:- The same method was used as above.

Yield:- 30 grams of ester.

30 grams of mesityn lactone.

This disproves Hembd's statement[1] that there is no mesityn

[1] Hembd, Thesis at Kiel, Ger. 1914.

lactone formed by this method.

B. Chlorination of the ester.

The first method to be tried was the chlorination of the ester by the reaction on it of chlorine in a carbon tetrachloride solution. The chlorine solution was prepared by allowing chlorine to pass thru carbon tetrachloride. When the solution had turned a distinct yellow it was standardized against sodium thiosulfate, using starch and potassium iodide as indicator. The calculated amount of solution containing the right amount of chlorine to react with 5 grams of the ester was then added to the ester in carbon tetrachloride and was then allowed to stand in the sunlight till there was no more free chlorine present. This determined by the use of starch- potassium iodide paper.

According to the literature[1] the chlorinated ester is crystalline. When there was no more free chlorine present the solvent was evaporated. The residue, instead of being crystalline, was an oil. Cooling, scratching the sides of the glass, and other methods were tried to make it crystallize, but to no avail.

Sulfuryl chloride as the chlorinating agent was then tried. The sulfuryl chloride at 0° was added to the ester at 0° in a solution of dry ether. It was allowed to stand at this temper-

[1] Annales de Chimie V. 24, Ser. 6, p. 98.

ature till all bubbling had ceased. The solution was allowed to stand at room temperature over night and the ether then distilled off. The result was an oil, and not the crystals that were wanted. This oil was distilled under diminished pressure. All of the liquid came over at 8 mm. pressure and 146° C. This is the temperature where the pure ester boils at that pressure. The distillate was tested for chlorine with a copper wire and the result was negative. It is therefore probable that the result was the unchanged ester and that no chlorination had taken place.

To determine whether the lack of chlorination might be due to impure sulfuryl chloride, the latter was distilled twice and the method tried again with no better results.

An attempt was then made to chlorinate the acid according to the method of Oppenheim and Precht given above[1]. It was thought that if it were possible to chlorinatethe acid, this chlor acid might be then esterified and the chlor ester obtained in that way.

Following the above mentioned method a mixture of the acid and chlorine in carbon tetrachloride was allowed to stand for half an hour. The solvent was then distilled off and the resulting crystals purified by throwing them out of chloroform with ligroin. The melting point (137°) of these crystals disclosed, however, that the acid had remained unchanged. Mixed melting

[1] This work, p. 5.

point with the pure acid--138° C. This method was then a failure.

The acid, however, was chlorinated by a modification of the above method. Instead of allowing the mixture of the acid and chlorine to stand for only a half hour it was allowed to stand for a week in sunlight. A small amount of iodine was present to catalyze the reaction. After a week the solvent was evaporated off and the resulting crystals melted at 94°. It was therefore the chlorinated acid. This compound is soluble in alcohol and water.

An esterification of the acid was tried using its silver salt and ethyl iodide. The silver salt was suspended in ether and the ethyl iodide added. The mixture was refluxed for eight hours and the solvent evaporated. Only a very small trace of the acid had been esterified.

IV

SUMMARY

In doing this work the original intention had been to chlorinate the ester and to determine the point in the ring where the chlorine entered. Owing, however, to the inability to obtain the chlorinated ester, the above object was not accomplished.

There were, however, some facts discovered that are worthy of note.

It was discovered that it is not necessary, in the preparation of the ester by the sulfuric acid method, to allow the mixture of sulfuric acid and acetoacetic ester to stand for fourteen days. Almost as good yields are obtained by allowing this mixture to stand four hours at a temperature of 35-40° C.

Allowing the first condensation product to stand twenty four hours after precipitation is unnecessary and does not increase the yield.

Contrary to Hembd's statements, mesityn lactone is formed in the hydrochloric acid method of preparation of the ester.

To chlorinate, the acid must be allowed to stand with a chlorine solution for a week in sunlight and in the presence of iodine.